Experimental Studies on the Pathogenesis of Bleeding from Esophageal Varices : with Special Reference to the Alteration of the Clo s ing Mechanism of Esophago-Gastric Junction

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by

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I. INTRODUCTION

Esophageal varices usually appear as a symptom of portal hypertension, and bleeding from ruptured varix often results in the fatal outcome. On such occasions, it is necessary not only to perform an emergency treatment for the hemorrhage, but also to consider a management of the underlying portal hypertension.[32)38)]

When esophageal varices are demonstrated, some prophylactic measures must be considered. Thus, studies for elucidating the pathogenetic factors are required both from the therapeutic and prophylactic points of view.

Various factors are mentioned as being related to bleeding of esophageal varices.[8)] However, it is highly controversial as to which of these factors does really play a leading role. Two major causes have been postulated ; the one is an increased hydrostatic pressure in the portal system and the other is injury of the esophageal mucosa due to acid-peptic digestion by the regurgitated gastric juice.[20)26)33)]

When varices involve the cardio-esophageal region, the sphincter mechanism at the cardio-esophageal junction is disturbed in the same way as the tension of the anal sphincter drops in case of hemorrhoids. Thus the gastric contents are allowed easily to leak back into the esophagus which has the lowest resistance against acid-peptic digestion and to remain there, and as a result the esophageal mucosa as well as varix wall are injured. Eventually, the possibility of rupture of varix may well be assumed.

For the purpose to clarify such insufficiency of the antireflux mechanism at the esophago-gastric junction following the occurrence of varices, the present author first undertook to produce esophageal varices artificially in dogs and compared the reflux of gastric contents into the esophagus in these dogs with that of the dogs in which their gastro-esophageal sphincter had been destroyed.

He examined the reflux on the experimental animals as well as on the patients with esophageal varices and compared with each other.

Thus the author studied the corelation between the alteration of gastroesophageal closing mechanism and rupture of varices.

II. EXPERIMENTAL PRODUCTION OF ESOPHAGEAL VARICES[15)19)22)23)28)35)36)]

A. Materials and Methods

Mongrel dogs weighing between 8 and 15 kilograms were subjected to surgical procedures designed to produce esophageal varices, with intravenously administered nembutal, 25 mg per kilogram. These procedures were performed in a 2-stage operation.

i) Portal Vein Constriction.[19)23)28)36)]

The dogs were subjected to right subcostal incision and had their portal vein trunk exposed, and, on the hepatic side of the superior pancreatico-duodenal vein, the portal vein was ligated with silver wire encased in vinyl tube to the extent that its diameter was reduced to 30～50% of the original circumference. In doing this, it was found to be convenient to have the vinyl tube set beforehand at the length of circumference assuring the desired extent of ligation. Here, also, the force of ligation was regulated to the extent that the color of the bowel did not have a tinge of extreme dark violet.

ii) Azygos Vein Ligation[19)28)36)]

Several weeks after the initial operation, endotracheal intubation and right thoracotomy were performed under a positive pressure respiration, and the right azygos vein was ligated at two points, as also were 2～3 intercostal veins which flowed into it between these two ligatures. In dogs, it was at the rate of 1 among 12 that the left azygos vein was in existence, and, accordingly, ligation of the right azygos vein only was assumed to be sufficient.

Several months after the constriction of the portal vein and the ligation of the azygos vein, laparotomy was performed under intravenous anesthesia, and by using 10～20 cc of 60% urografin, splenoportography was taken to examine the development of portal collaterals. IMANAGA[11)] holds that, when an image of coronary vein or short gastric vein is recognized in portal venogram, the existence of esophageal varices may be definitely assumed. In cases with highly marked development of esophageal collaterals, a gastroesophageal reflux test was performed. Finally, at post mortem examination, esophageal collaterals and esophageal mucosa were examined, macroscopically and histologically. Furthermore, blood was taken out of the dogs and irrigation was carried out with a physiologic saline solution, heated at about 40°C. Through the coronary vein, 10% gelatin-added India ink was injected, and the condition of submucous venous plexus in the esophageal and gastrocardiac zone was compared with that of normal dogs.

Moreover, as an attempt to make the development of esophageal varices still more marked, constriction of inferior vena cava and splenic arterio-venous shunt were added.

iii) Inferior Vena Cava Constriction[19)28)]

Together with the ligation of azygos vein, the inferior vena cava was constricted with silk thread supradiaphragmatically to about 1/2 of original diameter.

iv) Splenic Arterio-Venous Shunt[35)]

The spleen was removed and a side-to-side shunt was performed between the splenic artery and vein by means of an INOGUCHI's small vessel anastomosing apparatus.

B. Experimental Results

For experimental production of esophageal varices, surgical procedures were performed on 22 dogs.

i) Group of Dogs Subjected to Portal Vein Constriction and Azygos Vein Ligation[36)]

Of 15 dogs used, 5 died within 1 month after the second-stage operation. Of 10

dogs which survived for more than 1 month, splenoportogram was taken, India ink was injected, or, at autopsy, the development of esophageal collaterals was observed in 8 cases (80%). Splenoportography was performed in 8 cases, and, in 5 cases, an extensive image of collaterals running upwards through the coronary vein was noticed (Photo 1a, 1b, 2).

At autopsy, a significant dilatation and tortuosity of several lines of venous collaterals developed along the outer layers of the esophagus (Photo 3) and a slight dilatation of submucosal vein was seen (Photo 4). One dog, in which an outstanding short circuit (by-pass shunt) produced between the splenic and renal veins, failed to show esophageal collaterals, was again subjected to laparotomy and had this short circuit removed ; then splenoportography and autopsy revealed a marked development of esophageal collaterals.

In one case, which ended in death after a repetition of melena, findings of errosive esophagitis were noticed in the lower part of esophagus. In 4 other cases, India ink was injected into the portal system, the esophageal and gastric mucosa were seen to be uniformly colored, and the gastric submucous venous plexus was seen to continuously communicate to the esophageal submucous venous plexus beyond the esophagogastric junction.

This communication, however, was seen to be very thin and sparse in normal dogs. The gastric mucosa was colored, but esophageal mucosa was not.

ii) Group of Dogs Subjected to Portal Vein Constriction, Azygos Vein Ligation and Constriction of Inferior Vena Cava[19]

These procedures were performed in 3 cases, the result of which dilatation of the peri-esophageal veins and submucosal veins were seen to be slightly augmented (Photo 5).

iii) Group of Dogs Subjected to Azygos Vein Ligation, Inferior Vena Cava Constriction and Portal Vein Constriction[19][28]

The Procedures performed in ii) were reversed in order in 2 cases. It was seen that the growth of esophageal collaterals was strengthened to the same degree as seen in ii).

iv) Group of Dogs Subjected to Azygos Vein Ligation, Inferior Vena Cava Constriction, Portal Vein Constriction and Splenic Arterio-Venous Shunt

These procedures were performed in 2 cases. As a result, an obstruction of the anastomosed part was induced, and, consequently, the growth of collaterals was seen to amount to about the same degree as seen in iii).

III. EXPERIMENTAL STUDY ON GASTRO-ESOPHAGEAL REGURGITATION

(1) Esophageal Reflux Test in Dogs[18]

In dogs with esophageal varices, the possibility of reflux of the gastric contents into the esophagus through the esophagogastric junction was examined, and it was examined in comparison with the cases which had undergone the destruction of the gastroesophageal closing mechanism. Generally, the closing mechanism at the esophagogastric junction in dogs, is understood to be provided with a considerable extent of automaticity, irrespective of the action of extrinsic nerves.[6]

A. Materials

i) Dogs with Esophageal Varices

Portal vein constriction and azygos vein ligation were performed at two stages, and, splenoportography performed several months after operation demonstrated marked develop-

ment of esophageal collaterals.

ii) Dogs with Damaged Gastroesophageal Closing Mechanism

The gastroesophageal closing mechanism, assumed to participate in the prevention of reflux, was damaged.

iii) Dogs which underwent Antireflux Procedures

The gastroesophageal closing mechanism was destroyed, and furthermore, the gastric fundus was sutured to the left side of abdominal esophagus and abdominal surface of the diaphragm.

B. Methods

Report by KURAMOTO et al.[18] was referred to.

Intravenous anesthesia with nembutal, 25mg per kg, was performed on dogs that had fasted for 24 hours. An effort was made to keep the depth of anesthesia as constant as possible. In order to secure the airway, endotracheal intubation was carried out and median incision was performed, and then, a water manometer was connected with gastric cavity through the back wall of the gastric body. Then, a bowel forceps was installed at the first portion of duodenum to block gastric contents from duodenum, and then a colored physiologic saline solution, heated at about 38°C and added with green pigment, was injected into the stomach by the irrigator at the rate of about 500cc per minute ; the moment when the saline solution flowed into the esophagus was confirmed by esophagoscope, and the intragastric pressure at that same moment was determined. The value thus determined stood at the mid-point of respiratory excursion.

C. Results

i) Normal Dogs

First, esophageal reflux test was conducted on normal dogs. Measurement was carried out 3 times and the average value was adopted. The reflux pressure, on an average, was 192 mm H_2O (Tab. 1) (Fig. 1).

Tab. 1 Gastroesophageal reflux pressure in normal dogs

Dog	Reflux pressure (mmH_2O)
No. 6	138
No. 8	170
No. 11	245
No. 12	215
No. 13	273
No. 15	175
No. 17	200
No. 18	120
No. 19	155
No. 20	225
mean	192

ii) Dogs with Esophageal Varices

Esophageal reflux test was conducted on five dogs that had survived half a year or a year after operation for the production of esophageal varices. It was found that the reflux pressure was as low as 98 mm H_2O on an average (Tab. 2) (Fig. 1).

iii) Dogs with Damaged Gastroesophageal Closing Mechanism

As maintained by CROSS & KAY[5], the inferior esophageal constrictor, gastric oblique muscle, right crus of diaphragm and phrenoesophageal ligament along with the valvular mechanism related to the oblique angle of entry of esophagus to stomach and compression by gasbubble in stomach, form the so-called gastroesophageal closing mechanism, and they are assumed to participate in the prevention of reflux[3)14)16)18)29] (Fig. 2).

BOTHA[2], in his comprehensive study, concluded that the inferior esophageal constric-

Tab. 2 Gastroesophageal reflux pressure in dogs with esophageal varices

Dog	Reflux pressure (mmH_2O)
No. 5	84
No. 9	50
No. 13	120
No. 14	110
No. 15	125
mean	98

tor and the mucosal fold at the esophagogastric junction play a most important role in the prevention of reflux.

These antireflux factors, thus, were damaged, and resultant change of reflux pressure was observed. The circular muscle fibers in the esophago-gastric junction were vertically severed for about 2 cm in length on the side of lesser curvature, and the oblique muscle fibers were cut vertically for about 2 cm in length on the left side of the cardia. Moreover, the right crus of the diaphragm was cut for about 3 cm in length, in a radial direction from the esophagus on the left side of the esophagus, while the phrenoesophageal ligament was exfoliated about 2 cm in length upwards from its attached portion to the esophagus, and then the reflux test was carried out. It was found that the reflux pressure gradually declined, which eventually dropped

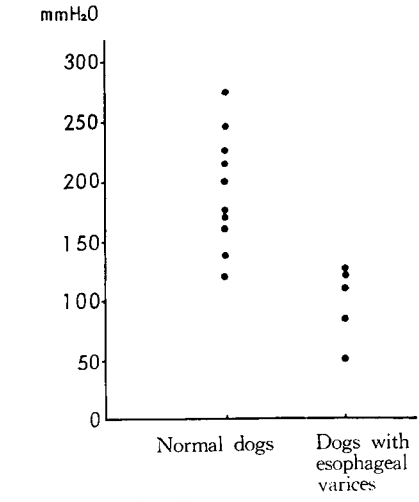

Fig. 1 Gastroesophageal reflux pressure

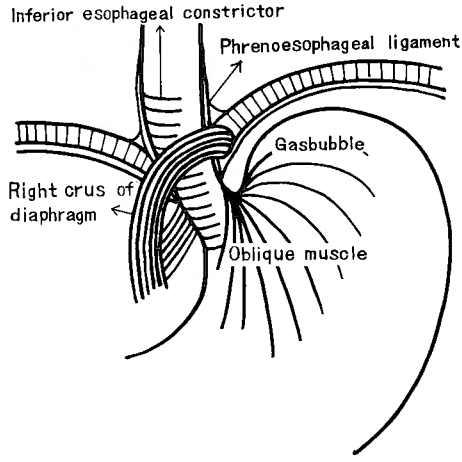

Fig. 2 Gastroesophageal closing mechanism

Tab. 3 Gastroesophageal reflux pressure (mmH_2O) after destruction of gastroesophageal closing mechanism and additional performance of antireflux procedure

Dog	Before treatment	Destruction of the gastroesophageal closing mechanism			Performance of antireflux procedure
		A	B	C	
No. 17	200	167	134	120	190
No. 18	120	110	80	43	120
No. 19	155	150	136	110	140
No. 20	225	155	105	70	235
mean	175	146	114	86	171

A : Severance of the circular muscle fibers
B : Severance of the oblique muscle fibers additionally
C : Severance of the right crus of diaphragm and exfoliation of the phreno-esophageal ligament additionally

to 86 mmH_2O on an average, approximately 50% of that of normal dogs (Tab. 3) (Fig. 3). The value was about the same as that of dogs with esophageal varices.

When the dogs were allowed to survive in this condition, several red errosive esophagitis were found to occur in the lower portion of the esophagus.

iv) Dogs which underwent Antireflux Procedures

In cases where the gastroesophageal sphincter was destroyed, and as a result, the reflux pressure had lowered, occurrence of esophagitis could be prevented when gastric fundus was sutured to the left side of the abdominal esophagus and abdominal surface of diaphragm and, thus, HIS' angle was made sharp as pointed out by STENSRUD et al.,[30)40)] (Fig. 4); the reflux pressure rose up to an

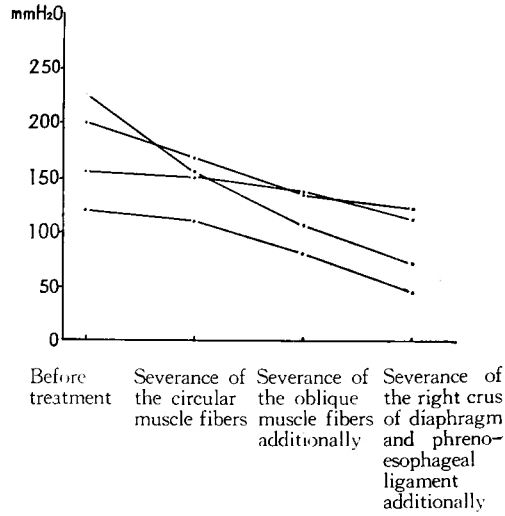

Fig. 3 Changes of gastroesophageal reflux pressure after destruction of gastroesophageal closing mechanism

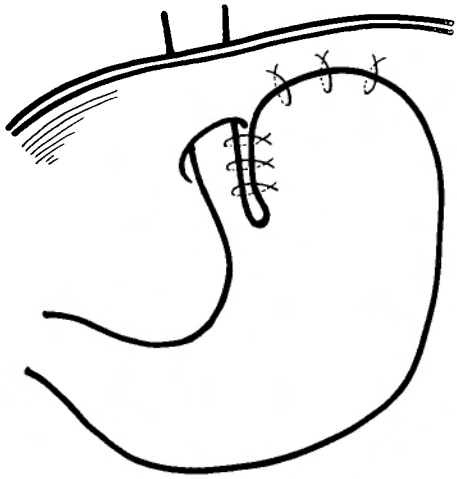

Fig. 4 Reconstruction of gastroesophageal closing mechanism by recreation of the esophagogastric angle ; gastric fundus was sutured to the left side of abdominal esophagus and abdominal surface of the diaphragm

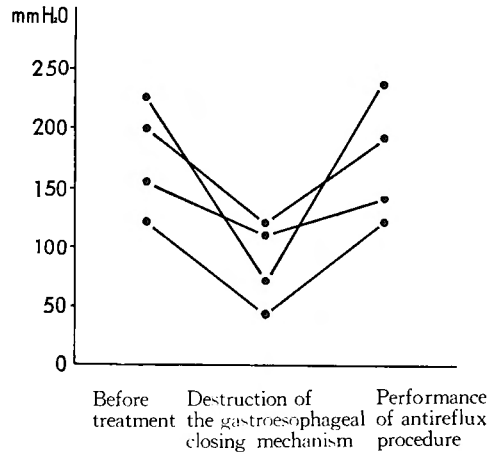

Fig. 5 Changes of gastroesophageal reflux pressure after destruction of gastroesophageal closing mechanism and additional performance of antireflux procedure

average value of 171 mmH_2O (Fig. 5) (Tab. 3), approximately the normal one. This surgical treatment for the prevention of reflux esophagitis[14)17)] may deserve a wide application in clinical cases.

(2) Esophageal Reflux Test in Clinical Cases

A. Materials and Methods

The patients with esophageal varices were given about 30cc of radiopaque media in a supine position, and after the radiopaque media entered into the stomach, they were examined whether there could be a reflux of radiopaque media from the stomach into the esophagus or not, with VALSALVA maneuver in TRENDELENBURG's position.

B. Results

First, esophageal reflux test was carried out fluoroscopically on 5 cases of normal men. No reflux of radiopaque media was noted.

Then, esophageal reflux test was performed on 5 cases of patients with esophageal varices (Photo 6a, 6b). Reflux of radiopaque media was always noted, and it was confirmed that the evacuation of radiopaque media from the esophagus was markedly retarded.

IV. INCIDENCES OF ESOPHAGEAL VARICES, BLEEDING VARICES AND ESOPHAGITIS IN THE PORTAL HYPERTENSION (Photo 7a, 7b)

In 95 autopsy cases with portal hypertension from the Pathological Department, Kyoto University Medical School, incidences of esophageal varices, bleeding varices[7)11)12)13)] and esophagitis were examined.

Esophageal varices were observed in 63 cases (66 %), and in 33 cases (52 %) of these, namely in 35% of the cases with portal hypertension, hematemesis was observed in their past history (Tab. 4). The present author investigated the concurrent existence of findings of esophagitis, i. e. redness, erosion and ulceration. In 32 cases of portal hypertension without esophageal varices, esophagitis was noted in only 5 cases (16%), while, in 63 cases of portal hypertension with esophageal varices, 30 cases (48%) indicated the findings of esophagitis. Particularly, in 33 cases of bleeding esophageal varices, 20 cases (61%) showed the pathologic picture of esophagitis (Tab. 5) (Fig. 6). Past reports[4)24)39)] show that findings of esophagitis were noted in 43.1 ~64% of the cases of bleeding esophageal varices.

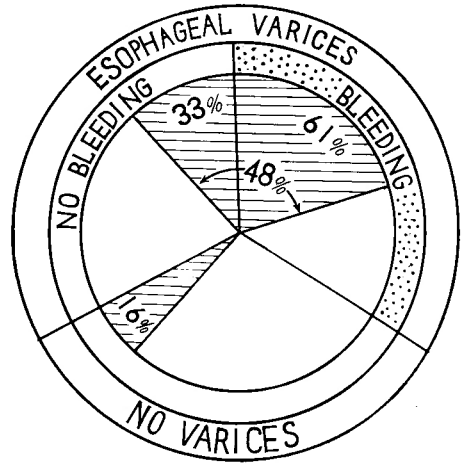

Fig. 6 Incidence of the esophagitis combined with portal hypertension

Tab. 4 Esophageal varices at autopsy among 95 patients with portal hypertension

Group	Intact varices %	Bleeding varices %	Total with varices %
Total : 95 patients	31	35	66
80 patients with cirrhosis of liver	31	33	64
11 patients with Banti's syndrome	18	55	73
4 patients with Budd-Chiari's syndrome	75	25	100

Tab. 5 Incidence of the esophagitis combined with portal hypertension

Group	Esophageal varices			Total
	−	+	Bleeding varices	
Total	5/32 (16%)	30/63 (48%)	20/33 (61%)	35/95 (37%)
Cirrhosis of liver	5/29	26/51	16/26	31/80
Banti's syndrome	0/3	3/8	3/6	3/11
Budd-Chiari's syndrome		1/1	1/1	1/4

V. RELATION BETWEEN THE VALUE OF PORTAL PRESSURE AND THE OCCURRENCE OF ESOPHAGEAL VARICES OR HEMATEMESIS (Fig. 7)

In recent cases of our clinic, the relation between the occurrence of bleeding esophageal varices and the value of portal pressure was examined. In cases with esophageal varices, generally, the portal pressure is slightly higher than the cases having no esophageal varices.[25] While, in cases with a history of hematemesis, the portal pressure is somewhat higher than the cases having no history of hematemesis. However, sometimes, portal pressure was seen to be relatively high even in the absence of esophageal varices, while on the other hand, history of hematemesis was seen to exist even in a case in which portal pressure remained relatively low. Esophageal varices with the same degree of portal hypertension gave in some cases a history of hematemesis, while in others not. In other words, the occurrence of hematemesis was not necessarily corelated to the intensity of portal hypertension, and, thus, the values of portal pressure showed no decisive parallel relationship to the occurrence of esophageal varices or bleeding varices.

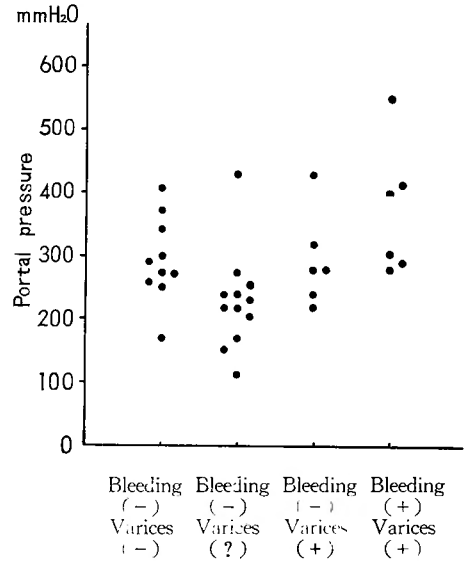

Fig. 7 Relation between the values of portal pressure and the occurrence of esophageal varices or hematemesis

VI. DISCUSSION

The experimental procedures to produce esophageal varices consist in the production of the same pathological changes in animals as seen in the clinical cases of BANTI's syndrome, liver cirrhosis and BUDD-CHIARI's syndrome. Various attempts have so far been undertaken in this line.

A monkey[19] is so akin to a human being that it would provide a highly convenient experimental animal for the production of such submucosal varices as often seen in human beings. However, monkeys are not easily available, and for this reason, dogs have usually been used for this purpose. When dogs are used as the experimental animals to produce

esophageal varices, the dilatation and tortuosity of periesophageal veins may easily occur, while dilated and varicose veins in the submucous layer as observed in the patients are scarcely brought about. Such a different pathologic picture of the esophageal veins in dogs from that of human beings may be due to the densely developed submucous tissue or to the specific arrangement of blood vessels in the esophageal region in the dog.[9)12)28)36)]

In the present study, in order to get the sufficient development of intraesophageal collaterals, the possible extraesophageal collateral ways were blocked : the portal vein trunk was constricted first, the azygos vein was ligated in two levels together with the several intercostal veins flowing into the blind segment of the azygos vein, and in some dogs, besides these procedures, the constriction of the inferior vena cava was added. As an attempt to make portal hypertension more marked, a shunt operation was devised between the splenic artery and vein, but it was unsuccessful because the shunt was obstructed by thrombus within several months. When gigantic collaterals were present between the splenic and renal vein in some experimental animals, the author had to remove them to get a sufficient development of collaterals in the esophagus.

In these dogs with esophageal varices, the gastric coronary vein, among many collaterals, indicated most distinct dilatation and tortuosity, and there were marked development of esophageal collaterals, running from cardia to diaphragm and esophagus. At the same time, the esophageal submucous venous plexus, likewise indicated dilatation, which was successively linked to the gastric submucous venous plexus at the esophago-gastric junction. Accordingly, the inferior esophageal constrictor, gastric oblique muscle, right crus of diaphragm and phrenoesophageal ligament, which constitute the gastroesophageal closing mechanism, under the influence of this esophageal collaterals, are assumed to undergo some damage. In fact, a test of reflux of the gastric contents into esophagus showed that, in cases of dogs with esophageal varices, reflux occurred as easily as when the gastroesophageal closing mechanism was experimentally destroyed.

On the other hand, in clinical cases of esophageal varices, roentgen examination clearly showed that the radiopaque media in the stomach easily make a reflux into the esophagus.

In the light of these experimental results it is known that when esophageal varices are brought about, an insufficiency is induced in the gastroesophageal closing mechanism and gastric contents make an easy reflux into the esophagus.

Also, at autopsy, it is worthy of notice that esophagitis were seen in 48 % of the cases with esophageal varices and in 61 % of the cases with bleeding esophageal varices (Fig. 6).

In patients with esophageal varices, roentgen examination frequently indicates dilatation of the esophageal lumen and retention of esophageal contents.[1)] By the retention of acid-peptic contents, germs, enzymes and their products, the esophagus would form an incubator, providing a base for the occurrence of esophagitis. Esophageal venous congestion, also, could be regarded as a factor for the onset of esophagitis.[16)]

That esophageal mucosa protein, on the other hand, shows an abnormally low resistance against acid-peptic digestion, has already been established by TAKATSUKI[34)] from our clinic. For this reason, an especially great emphasis is placed on the regurgitation of the acid-peptic gastric juice as a factor inducing esophagitis.

Furthermore a rise of intraabdominal pressure due to splenomegaly or ascites will facilitate gastric contents to leak back into the esophagus, and esophageal varices will do it, too, by destroying the closing mechanism of the esophago-gastric junction. The gastric contents, thus regurgitated, will injure the esophageal mucosa, because it is less resistant against acid-peptic digestion than the gastric mucosa.

When esophageal varices occur, they bulge into the lumen and the mucous epithelium becomes extremely thin (Photo 7a). Varices in the submucosa of esophagus, covered with such a thin membrane, are always exposed to danger of rupture and bleeding under the influence of mechanical stimuli of food passage, autodigestion by the regurgitated gastric juice, and the continuous fluctuation of intra-abdominal and intra-thoracic pressure [12]

In general, esophageal varices are induced by a continuation of severe portal hypertension, and the higher the degree of the portal hypertension the greater the diameter of varicose veins. The intravenous pressure causes constitutional and degenerative change of the venous walls and bring about tortuosity, partial swelling, and thinning of the venous walls.[37] Here, under the influence of vomiting, retching, coughing, straining, etc., the venous pressure may raise rapidly[20], then varices may happen to be ruptured. Also, the bleeding tendency and the rise of venous pressure in portal hypertension make it extremely difficult to stop bleeding once occurred and lead to profuse hemorrhage.

Although varices are frequently seen to occur not only in the esophageal submucous tissue but also in the cardial submucosa, phrenoesophageal membrane of the esophagus, subserosa under the coronary vein supply and retroperitoneum, rupture and resultant bleeding occur nearly always in esophageal submucosal varices. This fact suggests a special nature that exists in the esophageal mucous membrane overlying varices.

On the other hand, the incidence of bleeding from esophageal varices is not always parallel to the degree of portal tension.[31] Indeed, such rare cases are reported in which bleeding occurred from esophageal varices without portal hypertension.[27] Thus, it is considered that reflux esophagitis, accompanied by the erosion and ulceration of the esophageal mucosa may be a direct factor for the occurrence of bleeding varices.[26]

In 1945, BARANOFSKY & WANGENSTEEN claimed that bleeding esophageal varices in portal hypertension is the result of erosion coming from acid-peptic digestion, while WAGENKNECHT[39] and his co-workers, at autopsy of patients with bleeding esophageal varices, found the ulceration of esophageal wall overlying the varices in 19 (43.1%) of 44 autopsy cases. CHILES[4] and his coworkers, likewise, in a similar study, proved a fact that, in 80 autopsy cases who died of rupture of esophageal varices ulcerations involved the wall in 45 cases (56%) to a sufficient degree to be regarded as the primary cause of rupture. They concluded that increased hydrostatic pressure at times may cause spontaneous rupture and bleeding, but in a majority of cases ulceration is the complicating factor which accelerates perforation of the varix wall. However, some authors[20][24] have reported that bleeding varices can occur in cases who show the lack of gastric acid or who have undergone total gastrectomy, and that in some cases of bleeding varices, mucosae in other regions than the varices have remained normal.

However, even after total gastrectomy, digestive esophagitis due to bile-tryptic activity possibly occurs. Venous congestion and activation of cathepsin (auto-tissue protein split-

ing enzyme), occurring in a varix region, may help to act more powerful acid-peptic digestion on the esophagus wall than in the other parts.

In view of this, the counterevidences reported by some authors described above cannot be decisive ones. Probably, 2～3 factors cooperate in bringing about the massive hemorrhage. In the present study, special emphasis was placed on the fact that acid-peptic digestion of the esophageal mucosa due to a reflux of gastric juice stimulates occurrence of reflux esophagitis and formation of ulceration, injures the varix wall, and thus results in bleeding. Also, when reduction of portal pressure is insufficient and the portal pressure remains over 250 mmH_2O, as seen after the trans-esophageal ligation of varices as an emergency procedure for bleeding esophageal varices, addition of the above-mentioned antireflux procedure (Fig. 4) is believable to be one of the reasonable means for preventing the occurrence of reflux esophagitis and bleeding varices.

VII. SUMMARY

By using dogs, esophageal varices were experimentally produced. Constriction of portal vein, ligation of azygos vein and ligation of 2～3 intercostal veins were carried out at two stages. Along the outer layers of the esophagus, the venous collaterals were seen to indicate dilatation and tortuosity as well as dilatation of the esophageal submucosal vein. Furthermore, constriction of inferior vena cava and splenic arteriovenous shunt were additionally carried out, and, as a result, a still more remarkable development of esophageal collaterals was observed.

By using 5 cases of dogs with esophageal varices, an esophageal reflux test was performed to examine whether the gastric contents are liable to make a reflux into the esophagus or not. The test showed that the reflux pressure dropped to about 50% of the value of normal dogs or about the same extent as when the gastroesophageal closing mechanism was destroyed, while, in clinical cases of esophageal varices, roentgen examination indicated that, the gastric contents tended to make an easy reflux into the esophagus.

At pathological autopsy and in clinical cases, it was clarified that esophagitis is combined with bleeding esophageal varices at a rate of 61%, and that, bleeding esophageal varices do not necessarily occur in parallel with the degree of portal tension.

In view of the factors thus elucidated, it was emphasized that digestion of esophageal mucosa by reflux and retention of the acid-peptic gastric juice in esophagus may possibly induce rupture and bleeding of varices. Furthermore, it was pointed out that, in case reductive procedure of portal pressure is insufficient as a treatment for the control of bleeding from varices, additional performance of the antireflux procedure would be reasonable to prevent recurrence of hematemesis.

In concluding the present report, the present author wishes to express his deep gratitude to Prof. Dr. CHUJI KIMURA, for his kind guidance, and to instructor KOICHI ISHIGAMI, who has consistently provided warm encouragement and guidance. He also wishes to profoundly thank the staff personnel of the Pathological Department, Kyoto University Medical School, who were kind enough to make the data on pathological autopsy available.

An abstract of the present article was made public at the 6th meeting of the Kansai Section of the Japanese Association for Thoracic Surgery.

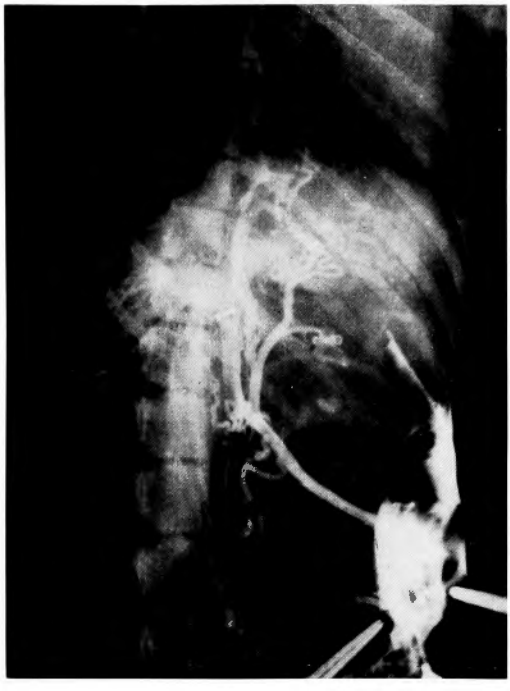

Photo 1. a Splenoportogram of dog No. 5 taken several months after operation shows extensive development of the esophageal collaterals.

Photo 1. b Splenoportogram of dog No. 5 taken 1 year after operation shows more extensive development of the collateral veins.

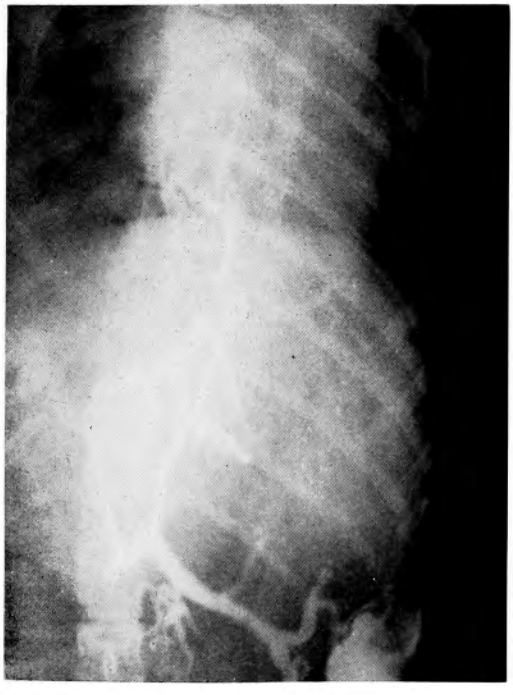

Photo 2 Splenoportogram of dog No. 9 taken 6 months after operation shows marked development of the esophageal varices.

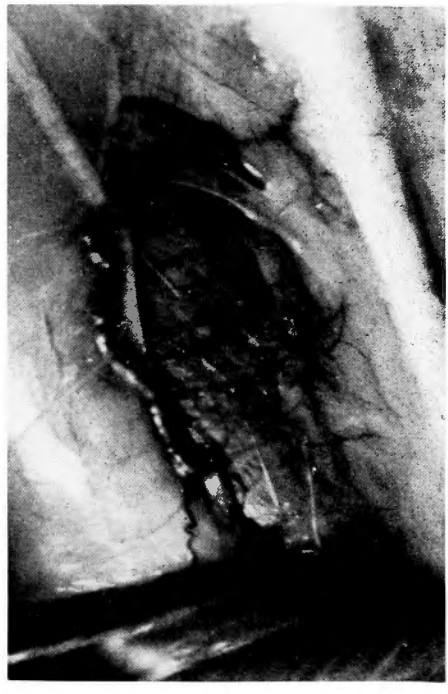

Photo 3 Gross appearance of varicose veins developed along the outer layers of the esophagus.

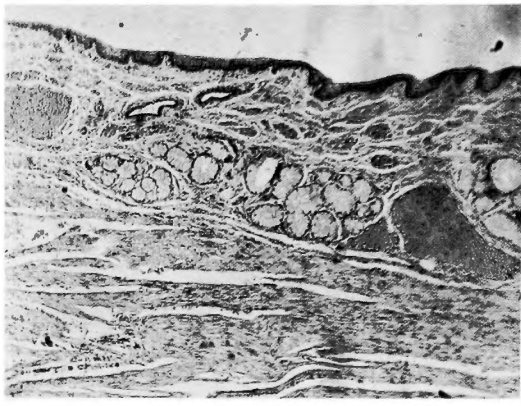

Photo 4 Histological appearance of the esophagus in an animal of group (i). Dilatation of the submucosal veins may be seen.

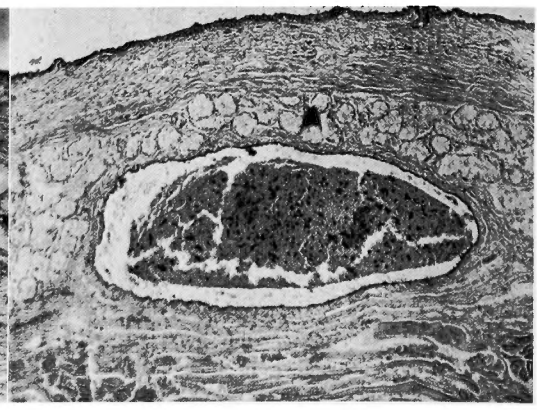

Photo 5 Histological appearance of the esophagus in an animal of group (ii). Marked dilatation of the submucosal veins may be seen.

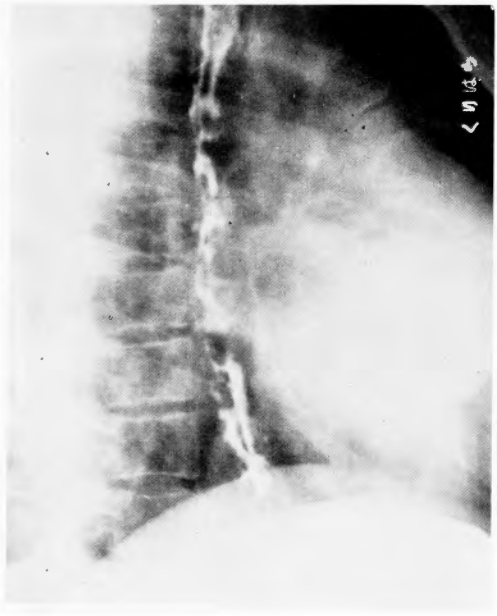

Photo 6. a Radiologic findings of the esophageal varices.

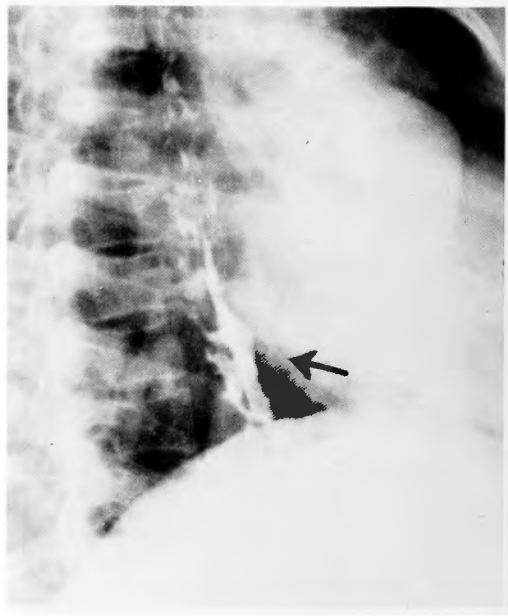

Photo 6. b Reflux of radiopaque media into the esophagus was demonstrated with the aid of Valsalva maneuver in a Trendelenburg's position.

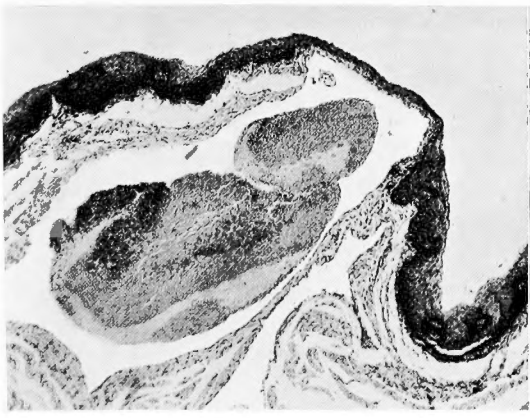

Photo 7. a Histological appearance of the esophagus in a patient with esophageal varices shows extremely thinning of the mucosa overlying the varices.

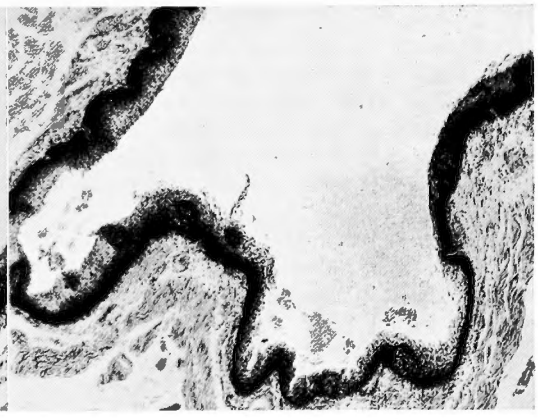

Photo 7. b Histological appearance of the esophagus in the same patient shows the discontinuity of the mucosa and the infiltration of inflammatory cells.

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和文抄録

食道静脈瘤の出血機転に関する実験的研究，とくに噴門括約筋機構の変化の意義について

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食道静脈瘤出血に関与する因子は種々あげられているが，どの因子が主役を演ずるかについては議論のある問題である．一方においては門脈系の静水力学的圧の上昇，他方においては胃液逆流に基く酸ペプシン性消化による食道粘膜の傷害という2つの重要な因子が考えられている．

食道・胃噴門部に静脈瘤が発生した場合には，あたかも痔核症の際に肛門括約筋緊張が低下するように，噴門括約筋機構が変化することが予想される．このような変化がおこると，胃内容が酸ペプシン消化に抵抗性の低い食道内へ容易に逆流・停滞して，食道粘膜および静脈瘤壁を傷害して，静脈瘤破裂を誘発する可能性が考えられる．

著者は食道静脈瘤の発生による噴門逆流防止機能の変化を実験的に明らかにするために，まず食道静脈瘤犬を実験的に作成し，それらにおける胃内容の食道内への逆流状態を噴門括約筋機構破壊犬と対比しながら実験的に検索し，また食道静脈瘤臨床例についても同様の検索を行ない，一方食道静脈瘤剖検例について逆流性食道炎合併の頻度を検討し，食道静脈瘤存在下における噴門括約筋機構の変化と静脈瘤破裂との関連性について研究し，次のような結果を得た．

(1) 22頭の犬を用いて実験的に食道静脈瘤作成を試みた．まず門脈狭窄，縦隔静脈結紮およびこれに流入する2,3の肋間静脈結紮を2次的に行ない，門脈撮影や剖検によつて食道外膜に沿う静脈副血行路の著明な拡張・蛇行，および食道粘膜下静脈の拡張をみとめた．更に下大静脈狭窄，脾動静脈吻合を追加したところ，一層強力な食道性副血行路の発育することを観察した．

(2) 食道静脈瘤犬5例を利用して，胃内容が食道内へ逆流し易いかどうかを検査するため，生食水を胃から食道内に逆流せしめるに要する内圧を測定した．逆流圧は正常犬における値の約50%までに低下し，丁度噴門括約筋機構を破壊した場合と同程度になつた．このように逆流圧が低下した場合，胃底部を腹部食道左側縁および横隔膜下面に縫着すると，逆流圧はほぼ正常値にまで上昇することをみとめた．

(3) 食道静脈瘤臨床例5例についてレ線透視検査で骨盤高位，Valsalva法を行なわせると，正常人とは異なつて，胃内容が食道内へ逆流し易く，かつ食道内に停滞し易いことを確認した．

(4) 95例の門脈圧亢進症の病理剖検例について，食道静脈瘤の症例63例のうち30例（48%）に発赤，糜爛，潰瘍等の食道炎の所見をみとめた．とくに食道静脈瘤性出血例33例中20例（61%）に食道炎が合併することをみとめた．

(5) 外科臨床例について食道静脈瘤出血は必ずしも門脈圧亢進の程度と平行しないことをみとめた．

(6) 以上の諸点から，酸ペプシン性胃液の逆流・停滞による食道粘膜の消化が静脈瘤破裂出血を誘発する可能性が考えられ，従つて食道静脈瘤出血の治療に際して，門脈減圧手術の効果が不十分の場合には，吐血再発の予防として前述の逆流防止術を追加することが合理的であると考えられる．